

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Morrison et al.

Art Unit: Not yet assigned

Application No. Not yet assigned

Filed: Herewith

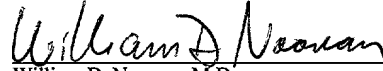
For: NUCLEIC ACIDS FOR DETECTING  
ASPERGILLUS SPECIES AND OTHER  
FILAMENTOUS FUNGI

Examiner: Not yet assigned

Date: January 14, 2002

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BOX PATENT APPLICATION  
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WASHINGTON, D.C. 20231

**PRELIMINARY AMENDMENT**

Prior to examination of the above-referenced application, please amend the application as follows:

**In the specification:**

On page 1, after the title, please insert the following new paragraph:

**--Priority Claim**

This is a divisional of U.S. Patent Application No. 09/423,233 filed June 27, 2000, which is a § 371 national stage of PCT/US98/08926 filed May 1, 1997, in turn claims the benefit of U.S. Provisional Application No. 60/045,400 filed May 2, 1997.--

Please add the following abstract as page 44 of the specification:

## NUCLEIC ACIDS FOR DETECTING *ASPERGILLUS* AND OTHER FILAMENTOUS FUNGI

### Abstract

Nucleic acids for detecting *Aspergillus* species and other filamentous fungi are provided. Unique internal transcribed space 2 coding regions permit the development of nucleic acid probes specific for five different species of *Aspergillus*, three species of *Fusarium*, four species of *Mucor*, two species of *Penicillium*, five species of *Rhizopus*, one species of *Rhizomucor*, as well as probes for *Absidia corymbifer*, *Cunninghamella elagans*, *Pseudallescheria boydii*, and *Sporothrix schenkii*. Methods are disclosed for the species-specific detection and diagnosis of infection by *Aspergillus*, *Fusarium*, *Mucor*, *Penicillium*, *Rhizomucor*, *absidia*, *Cunninghamella*, *Pseudallescheria* or *Sporothrix* in a subject. Furthermore, genus-specific probes are also provided for *Aspergillus*, *Fusarium* and *Mucor*, in addition to an all-fungus nucleic acid probe.

### In the claims:

Please amend the claims as follows:

1. (Amended) An isolated nucleic acid probe that consists essentially of 10 to 50 consecutive nucleotides for species-specific identification of *Fusarium*, wherein the probe hybridizes to the internal transcribed spacer 2 nucleic acid sequence of *Fusarium solani* (SEQ ID NO:6), or *Fusarium moniliforme* (SEQ ID NO:7), but does not hybridize to the internal transcribed space 2 nucleic acid sequence of *Aspergillus flavus* (SEQ ID NO:1), *Aspergillus fumigatus* (SEQ ID NO:2), *Aspergillus niger* (SEQ ID NO:3), *Aspergillus terreus* (SEQ ID NO:4), or *Aspergillus nidulans* (SEQ ID NO:5), *Mucor rouxii* (SEQ ID NO:8), *Mucor racemosus* (SEQ ID NO:9), *Mucor plumbeus* (SEQ ID NO:10), *Mucor indicus* (SEQ ID NO:11), *Mucor circinilloides f. circinelloides* (SEQ ID NO:12), *Rhizopus oryzae* (SEQ ID NO:13 and NO:14), *Rhizopus microsporus* (SEQ ID NO:15 and 16), *Rhizopus circinans* (SEQ ID NO:17 and 18), *Rhizopus stolonifer* (SEQ ID NO: 19), *Rhizomucor pusillus* (SEQ ID NO:20), *Absidia corymbifera* (SEQ ID NO:21 and 22), *Cunninghamella elegans* (SEQ ID NO:23), *Pseudallescheria boydii* (teleomorph of *Scedosporium apiospermum*) (SEQ ID NO:24, 25, 26, and 27), *Penicillium notatum* (SEQ ID NO:28), or *Sporothrix schenkii* (SEQ ID NO:29) .

Please cancel claims 2-6, without prejudice.

7. (Amended) The isolated nucleic acid probe of Claim 1 wherein the probe selectively hybridizes with a *Fusarium solani* nucleic acid of SEQ ID NO:6, or a complementary sequence thereof.

8. (Amended) The isolated nucleic acid probe of Claim 1 wherein the probe selectively hybridizes with a *Fusarium moniliforme* of SEQ ID NO:7, or a complementary sequence thereof.

Please cancel claims 9-23, without prejudice.

24. (Amended) A method of detecting a species of *Fusarium solani* (SEQ ID NO:6) or *Fusarium moniliforme* (SEQ ID NO:7), in a sample comprising contacting the sample with a nucleic acid probe consisting essentially of 10 to 50 consecutive nucleotides that selectively hybridizes with a nucleic acid having a sequence as set forth as SEQ ID NO:5 or SEQ ID NO:6, or a complementary sequence thereof; wherein hybridization of the nucleic acid probe with the sample indicates the detection of the *Fusarium* species in the sample.

Please cancel claims 25-29, without prejudice.

30. (Amended) The method of Claim 24, wherein the probe selectively hybridizes with a *Fusarium solani* nucleic acid of SEQ ID NO:6, or a complementary sequence thereof.

31. (Amended) The method of Claim 24, wherein the probe selectively hybridizes with a *Fusarium moniliforme* of SEQ ID NO:7, or a complementary sequence thereof.

Please cancel claims 34-46.

47. (Amended) An isolated nucleic acid probe for identifying a member of a *Fusarium* genus wherein the probe consists essentially of a nucleotide sequence as set forth as SEQ ID NO:59, or a complementary sequence thereof, respectively.

Please cancel claim 48.

49. (Amended) A method for detecting a member of a *Fusarium* genus in a sample, comprising

combining the sample with a nucleic acid probe that selectively hybridizes with a portion of the nucleic acid of SEQ ID NO:59, or a complementary sequence thereof, respectively, wherein hybridization of the probe with the sample indicates the presence of *Fusarium* in the sample.

Please add the following new claims:

51. (New) An isolated nucleic probe that hybridizes to an internal transcribed spacer 2 region of a *Fusarium* species, wherein the probe consists essentially of a nucleic acid sequence having a sequence as set forth as SEQ ID NO:49, SEQ ID NO:50, or SEQ ID NO:51, and wherein the probe does not hybridize to but does not hybridize to the internal transcribed space 2 nucleic acid sequence of *Aspergillus flavus* (SEQ ID NO:1), *Aspergillus fumigatus* (SEQ ID NO:2), *Aspergillus niger* (SEQ ID NO:3), *Aspergillus terreus* (SEQ ID NO:4), or *Aspergillus nidulans* (SEQ ID NO:5), *Mucor rouxii* (SEQ ID NO:8), *Mucor racemosus* (SEQ ID NO:9), *Mucor plumbeus* (SEQ ID NO:10), *Mucor indicus* (SEQ ID NO:11), *Mucor circinilloides f. circinelloides* (SEQ ID NO:12), *Rhizopus oryzae* (SEQ ID NO:13 and NO:14), *Rhizopus microsporus* (SEQ ID NO:15 and 16), *Rhizopus circinans* (SEQ ID NO:17 and 18), *Rhizopus stolonifer* (SEQ ID NO: 19), *Rhizomucor pusillus* (SEQ ID NO:20), *Absidia corymbifera* (SEQ ID NO:21 and 22), *Cunninghamella elegans* (SEQ ID NO:23), *Pseudallescheria boydii* (teleomorph of *Scedosporium apiospermum*) (SEQ ID NO:24, 25, 26, and 27), *Penicillium notatum* (SEQ ID NO:28), or *Sporothrix schenkii* (SEQ ID NO:29).

52. (New) The isolated nucleic probe of Claim 1, wherein the probe consists essentially of a nucleic acid sequence having a sequence as set forth as SEQ ID NO:49.

53. (New) The isolated nucleic probe of Claim 1, wherein the probe consists essentially of a nucleic acid sequence having a sequence as set forth as SEQ ID NO:50.

54. (New) The isolated nucleic probe of Claim 1, wherein the probe consists essentially of a nucleic acid sequence having a sequence as set forth as SEQ ID NO:51.

55. (New) The method of Claim 24, wherein the probe consists essentially of a nucleic acid sequence having a sequence as set forth as SEQ ID NO:49.

56. (New) The method of Claim 24, wherein the probe consists essentially of a nucleic acid sequence having a sequence as set forth as SEQ ID NO:50.

57. (New) The method of Claim 24, wherein the probe consists essentially of a nucleic acid sequence having a sequence as set forth as SEQ ID NO:51.

58. (New) A isolated nucleic acid sequence comprising a sequence as set forth as SEQ ID NO:5 or SEQ ID NO:6.

59. (New) A isolated nucleic acid sequence consisting essentially of a sequence as set forth as SEQ ID NO:5 or SEQ ID NO:6.

#### REMARKS

This Preliminary Amendment is submitted to enter Applicants' claims of priority from corresponding U.S. Patent Application No. 09/423,233 filed June 27, 2000, which is a § 371 national stage of PCT/US98/08926 filed May 1, 1997, in turn claims the benefit of U.S. Provisional Application No. 60/045,400 filed May 2, 1997. In addition, the specification is amended to include the abstract submitted in the PCT as a separate page.

Claims 1, 7, 8, 24,30-31, 47, and 49 are amended herein to correct form. Support for the amending language of these claims can be found throughout the specification, specifically on page 4, lines 4-22, page 5, lines 16 to page 7, lines 27. New claims 51-59 are added. Support for new claims 51-59 can be found throughout the specification, specifically on page 4, lines 4-22,

page 5, lines 16 to page 7, lines 27, on page 22 (Table 2), and on page 25, line 2 to page 27, line 4.

Claims 2-6, 9-23, 25-29, 34-46, 48, and 50 are canceled solely in order to reduce the filing fees. Applicants reserve the right to pursue the subject matter of these claims in a continuation application.

No new matter is added.

### CONCLUSION

If any minor matters remain to be discussed prior to examination, the Examiner is invited to contact the undersigned at the telephone number listed below.

Respectfully submitted,

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**Marked-up Version of Amended Specification and Claims  
Pursuant to 37 C.F.R. §§ 1.121(b)-(c)**

**In the specification:**

On page 1, after the title, please insert the following new paragraph:

**Priority Claim**

This is a divisional of U.S. Patent Application No. 09/423,233 filed June 27, 2000, which is a § 371 national stage of PCT/US98/08926 filed May 1, 1997, in turn claims the benefit of U.S. Provisional Application No. 60/045,400 filed May 2, 1997.

Please add the following abstract as page 44 of the specification:

**NUCLEIC ACIDS FOR DETECTING *ASPERGILLUS*  
AND OTHER FILAMENTOUS FUNGI**

**Abstract**

Nucleic acids for detecting *Aspergillus* species and other filamentous fungi are provided. Unique internal transcribed space 2 coding regions permit the development of nucleic acid probes specific for five different species of *Aspergillus*, three species of *Fusarium*, four species of *Mucor*, two species of *Penecillium*, five species of *Rhizopus*, one species of *Rhizomucor*, as well as probes for *Absidia corymbifer*, *Cunninghamella elagans*, *Pseudallescheria boydii*, and *Sporothrix schenkii*. Methods are disclosed for the species-specific detection and diagnosis of infection by *Aspergillus*, *Fusarium*, *Mucor*, *Penecillium*, *Rhizomucor*, *absidia*, *Cunninghaemella*, *Pseudallescheria* or *Sporthrix* in a subject. Furthermore, genus-specific probes are also provided for *Aspergillus*, *Fusarium* and *Mucor*, in addition to an all-fungus nucleic acid probe.

**In the claims:**

Please amend the claims as follows:

1. (Amended) [The isolated nucleic acid probe of claim 51] An isolated nucleic acid probe that consists essentially of 10 to 50 consecutive nucleotides for species-specific identification of *Fusarium*, wherein the probe hybridizes to the internal transcribed spacer 2 nucleic acid sequence [is selected from the group consisting of [*Aspergillus flavus* (SEQ ID NO:1), *Aspergillus fumigatus* (SEQ ID NO:2), *Aspergillus niger* (SEQ ID NO:3), *Aspergillus terreus* (SEQ ID NO:4), *Aspergillus nidulans* (SEQ ID NO:5)], *Fusarium solani* (SEQ ID NO:6) [.] or *Fusarium moniliforme* (SEQ ID NO:7), but does not hybridize to the internal transcribed space 2 nucleic acid sequence of *Aspergillus flavus* (SEQ ID NO:1), *Aspergillus fumigatus* (SEQ ID NO:2), *Aspergillus niger* (SEQ ID NO:3), *Aspergillus terreus* (SEQ ID NO:4), *Aspergillus nidulans* (SEQ ID NO:5), *Mucor rouxii* (SEQ ID NO:8), *Mucor racemosus* (SEQ ID NO:9), *Mucor plumbeus* (SEQ ID NO:10), *Mucor indicus* (SEQ ID NO:11), *Mucor circinilloides f. circinelloides* (SEQ ID NO:12), *Rhizopus oryzae* (SEQ ID NO:13 and NO:14), *Rhizopus microsporus* (SEQ ID NO:15 and 16), *Rhizopus circinans* (SEQ ID NO:17 and 18), *Rhizopus stolonifer* (SEQ ID NO: 19), *Rhizomucor pusillus* (SEQ ID NO:20), *Absidia corymbifera* (SEQ ID NO:21 and 22), *Cunninghamella elegans* (SEQ ID NO:23), *Pseudallescheria boydii* (teleomorph of *Scedosporium apiospermum*) (SEQ ID NO:24, 25, 26, and 27), *Penicillium notatum* (SEQ ID NO:28), or *Sporothrix schenkii* (SEQ ID NO:29) [wherein the probe selectively hybridizes to a portion of at least one of the nucleic acid of SEQ ID NOS:1-29, or a complementary sequence thereof, respectively] .

Please cancel claims 2-6.

7. (Amended) The isolated nucleic acid probe of Claim 1 [capable of] wherein the probe selectively [hybridizing] hybridizes with a *Fusarium solani* nucleic acid of SEQ ID NO:6, or a complementary sequence thereof.

8. (Amended) The isolated nucleic acid probe of Claim 1 [capable of] wherein the probe selectively [hybridizing] hybridizes with a *Fusarium moniliforme* of SEQ ID NO:7, or a complementary sequence thereof.

Please cancel claims 9-23.

24. (Twice amended) A method of detecting a species of [filamentous fungi selected from the group consisting of *Aspergillus [flavus* (SEQ ID NO:1), *Aspergillus fumigatus* (SEQ ID NO:2)], *Aspergillus niger* (SEQ ID NO:3), *Aspergillus terreus* (SEQ ID NO:4), *Aspergillus nidulans*

(SEQ ID NO:5), *Fusarium solani* (SEQ ID NO:6) or *Fusarium moniliforme* (SEQ ID NO:7), *Mucor rouxii* (SEQ ID NO:8), *Mucor racemosus* (SEQ ID NO:9), *Mucor plumbeus* (SEQ ID NO:10), *Mucor indicus* (SEQ ID NO:11), *Mucor circinilloides f. circinelloides* (SEQ ID NO:12), *Rhizopus oryzae* (SEQ ID NO:13 and NO:14), *Rhizopus microsporus* (SEQ ID NO:15 and 16), *Rhizopus circinans* (SEQ ID NO:17 and 18), *Rhizopus stolonifer* (SEQ ID NO: 19), *Rhizomucor pusillus* (SEQ ID NO:20), *Absidia corymbifera* (SEQ ID NO:21 and 22), *Cunninghamella elegans* (SEQ ID NO:23), *Pseudallescheria boydii* (teleomorph of *Scedosporium apiospermum*) (SEQ ID NO:24, 25, 26, and 27), *Penicillium notatum* (SEQ ID NO:28), or *Sporothrix schenkii* (SEQ ID NO:29)] in a sample comprising

contacting the sample with a nucleic acid probe consisting essentially of 10 to 50 consecutive nucleotides that selectively hybridizes with [at least one of] a nucleic acid [of SEQ ID NO:1-29] having a sequence as set forth as SEQ ID NO:5 or SEQ ID NO:6, or a complementary sequence thereof, respectively];

wherein hybridization of the nucleic acid probe with the sample indicates the detection of the *Fusarium* species in the sample.

Please cancel claims 25-29.

30. (Amended) The method of Claim 24, wherein the probe [is capable of] selectively [hybridizing] hybridizes with a *Fusarium solani* nucleic acid of SEQ ID NO:6, or a complementary sequence thereof.

31. (Amended) The method of Claim 24, wherein the probe [is capable of] selectively [hybridizing] hybridizes with a *Fusarium moniliforme* of SEQ ID NO:7, or a complementary sequence thereof.

Please cancel claims 34-46.

47. (Amended) An isolated nucleic acid probe for identifying a member of a [genus selected from the group consisting of *Aspergillus*,] *Fusarium* genus [and *Mucor*] wherein the probe [selectively hybridizes to a portion of a nucleic acid having a sequence as set forth as of SEQ ID

NOS:58-60,] consists essentially of a nucleotide sequence as set forth as SEQ ID NO:59, or a complementary sequence thereof, respectively.

Please cancel claim 48.

49. (Amended) A method for detecting a member of a [genus selected from the consisting of *Aspergillus*,] *Fusarium* genus [and *Mucor*] in a sample, comprising combining the sample with a nucleic acid probe [capable of] that selectively [hybridizing] hybridizes with a portion of the nucleic acid of [of SEQ ID NOS:58-60] SEQ ID NO:59, or a complementary sequence thereof, respectively, [the presence of hybridization indicating the detection of the respective genus] wherein hybridization of the probe with the sample indicates the presence of *Fusarium* in the sample.

Please add the following new claims:

51. (New) An isolated nucleic probe that hybridizes to an internal transcribed spacer 2 region of a *Fusarium* species, wherein the probe consists essentially of a nucleic acid sequence having a sequence as set forth as SEQ ID NO:49, SEQ ID NO:50, or SEQ ID NO:51, and wherein the probe does not hybridize to but does not hybridize to the internal transcribed space 2 nucleic acid sequence of *Aspergillus flavus* (SEQ ID NO:1), *Aspergillus fumigatus* (SEQ ID NO:2), *Aspergillus niger* (SEQ ID NO:3), *Aspergillus terreus* (SEQ ID NO:4), or *Aspergillus nidulans* (SEQ ID NO:5), *Mucor rouxii* (SEQ ID NO:8), *Mucor racemosus* (SEQ ID NO:9), *Mucor plumbeus* (SEQ ID NO:10), *Mucor indicus* (SEQ ID NO:11), *Mucor circinilloides f. circinelloides* (SEQ ID NO:12), *Rhizopus oryzae* (SEQ ID NO:13 and NO:14), *Rhizopus microsporus* (SEQ ID NO:15 and 16), *Rhizopus circinans* (SEQ ID NO:17 and 18), *Rhizopus stolonifer* (SEQ ID NO: 19), *Rhizomucor pusillus* (SEQ ID NO:20), *Absidia corymbifera* (SEQ ID NO:21 and 22), *Cunninghamella elegans* (SEQ ID NO:23), *Pseudallescheria boydii* (teleomorph of *Scedosporium apiospermum*) (SEQ ID NO:24, 25, 26, and 27), *Penicillium notatum* (SEQ ID NO:28), or *Sporothrix schenkii* (SEQ ID NO:29).

52. (New) The isolated nucleic probe of Claim 1, wherein the probe consists essentially of a nucleic acid sequence having a sequence as set forth as SEQ ID NO:49.

53. (New) The isolated nucleic probe of Claim 1, wherein the probe consists essentially of a nucleic acid sequence having a sequence as set forth as SEQ ID NO:50.

54. (New) The isolated nucleic probe of Claim 1, wherein the probe consists essentially of a nucleic acid sequence having a sequence as set forth as SEQ ID NO:51.

55. (New) The method of Claim 24, wherein the probe consists essentially of a nucleic acid sequence having a sequence as set forth as SEQ ID NO:49.

56. (New) The method of Claim 24, wherein the probe consists essentially of a nucleic acid sequence having a sequence as set forth as SEQ ID NO:50.

57. (New) The method of Claim 24, wherein the probe consists essentially of a nucleic acid sequence having a sequence as set forth as SEQ ID NO:51.

58. (New) A isolated nucleic acid sequence comprising a sequence as set forth as SEQ ID NO:5 or SEQ ID NO:6.

59. (New) A isolated nucleic acid sequence consisting essentially of a sequence as set forth as SEQ ID NO:5 or SEQ ID NO:6.